K000005

MAR - 3 2000

510 (k) Summary
Safety and Effectiveness

This summary of safety and effectiveness information has been prepared in accordance with the requirements of SMDA 1990 and 21 CFR Part 807.92.

Name: **Address:**	Diagnostic Products Corporation 5700 West 96th Street Los Angeles, CA 90045
Telephone Number: **Facsimile Number:**	(310) 645-8200 (310) 645-9999
Contact Person:	Edward M. Levine, Ph.D. Director of Clinical Affairs
Date of Preparation:	December 27, 1999
Device Name: Trade:	IMMULITE® Valproic Acid and IMMULITE® 2000 Valproic Acid
Catalog Number:	LKVA1 (100 tests), LKVA5 (500 tests) L2KVA1 (200 tests), L2KVA6 (600 tests)
CFR:	A neuroleptic drugs radioceptor assay test system is a device intended to measure in serum or plasma the dopamine receptor blocking activity of neuroleptic drugs and their active metabolites. A neuroleptic drug has anti-psychotic action affecting principally psychomotor activity, is generally without hypnotic effects, and is a tranquilizer. Measurements obtained by this device are used to aid in determining whether a patient is taking the prescribed dosage level of such drugs.
Common:	Reagent system for the determination of valproic acid in serum or heparinized plasma
Classification:	Class II device, 91-LEG (21 CFR 862.3645)
Panel:	Toxicology
CLIA Complexity Category:	We believe the category to be moderate, based on previous classification of analogous tests.

Manufacturer:	Diagnostic Products Corporation (DPC) 5700 West 96th Street Los Angeles, CA 90045-5597
Establishment Registration #:	DPC's establishment Registration No. is 2017183
Substantially Equivalent Predicate Device:	Abbott TDxFLx Valproic Acid (K904226)
Description of Device:	IMMULITE® Valproic Acid and IMMULITE® 2000 Valproic Acid are solid-phase, chemiluminescent enzyme immunometric assays for use with their respective IMMULITE® / IMMULITE® 2000 Automated Analyzers.
Intended Use of the Device:	IMMULITE® Valproic Acid and IMMULITE® 2000 Valproic Acid are for use with their respective IMMULITE and IMMULITE® 2000 analyzers for the quantitative measurement of valproic acid in serum or heparinized plasma, as an aid in monitoring drug therapy.

Technology

This section does not contain any new information for a reviewer who is familiar with the DPC IMMULITE System based upon the review of previous IMMULITE assay submissions.

IMMULITE Valproic Acid is a solid-phase, chemiluminescent immunometric assay. The solid-phase, a polystyrene bead enclosed within a IMMULITE Test Unit, is coated with a monoclonal murine antibody specific for valproic acid.

The patient sample and alkaline phosphatase-conjugated valproic acid are simultaneously introduced into the Test Unit and incubated for approximately 30 minutes at 37 °C with intermittent agitation. During this time, valproic acid in the samples competes with enzyme-labeled valproic acid for a limited number of antibody binding sites on the bead. Unbound enzyme conjugate is then removed by a centrifugal wash, after which substrate is added and the Test Unit is incubated for a further 10 minutes.

The chemiluminescent substrate, a phosphate ester of adamantyl dioxetane, undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. The continuous production of this intermediate results in the sustained emission of light, thus improving precision by providing a window for multiple readings. The bound complex - and thus also the photon output, as measured by the luminometer - is proportional to the concentration of valproic acid in the sample.

IMMULITE 2000 Valproic Acid is a solid-phase, chemiluminescent immunoassay. The solid-phase, a polystyrene bead, is coated with a polyclonal antibody specific for valproic acid.

The patient sample and alkaline phosphatase-conjugated valproic acid are simultaneously introduced into the Reaction Tube and incubated for approximately 30 minutes at 37 °C with intermittent agitation. During this time, valproic acid in the samples competes with enzyme-labeled carbamazepine for a limited number of antibody binding sites on the bead. Unbound enzyme conjugate is then removed by a centrifugal wash, after which substrate is added and the Reaction Tube is incubated for an additional 5 minutes.

The chemiluminescent substrate, a phosphate ester of adamantyl dioxetane, undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. The continuous production of this intermediate results in the sustained emission of light, thus improving precision by providing a window for multiple readings. The bound complex - and thus also the photon output, as measured by the luminometer - is inversely proportional to the concentration of valproic acid in the sample.

Abbott TDxFLx Valproic Acid utilizes fluorescence polarization immunoassay technology in a competitive ligand format. The unlabeled drug (antigen being measured) competes with the fluorescent-labeled antigen for the antibody binding sites. With increasing concentration of unlabeled antigen, more fluorescent-labeled antigen becomes unbound. Therefore, the fluorescent polarization signal decreases as the drug concentration increases, as measured by the fluorometer. Concentrations are determined from a stored standard curve.

Performance Equivalence

Diagnostic Products Corporation asserts that the IMMULITE Valproic Acid and IMMULITE 2000 Valproic Acid assays produce substantially equivalent results to other commercially marketed valproic Acid assays, such as Abbott TDxFLx Valproic Acid. The Abbott TDxFLx Valproic Acid assay utilizes fluorescence polarization technology. Each product is designed for the quantitative measurement of valproic acid in serum or heparinized plasma. Each product is intended strictly for in vitro diagnostic use as an aid in monitoring the therapeutic administration of this drug.

Method Comparison

The IMMULITE Valproic Acid procedure was compared to a commercially available assay for valproic acid (Abbott TDxFLX) on 48 patient samples, with valproic acid concentrations ranging from approximately 19 to 144 µg/mL. Linear regression analysis yielded the following statistics:

(IMMULITE) = 1.0 (Abbott) + 2.7 µg/mL r = 0.983

Means: 71 µg/mL (IMMULITE)
68 µg/mL (Abbott)

The IMMULITE 2000 Valproic Acid procedure was compared to DPC's IMMULITE Valproic Acid on 50 samples, with valproic acid concentrations ranging from approximately 24 to 180 µg/mL. Linear regression yielded the following statistics.

(IML2000) = 1.0 (IML) - 0.46 µg/mL r = 0.998

Means: 81 µg/mL (IMMULITE 2000)
82 µg/mL (IMMULITE)

Conclusion:

The data presented in this summary of safety and effectiveness is the data that the Food and Drug Administration used in granting DPC substantial equivalence for IMMULITE® Valproic Acid and for IMMULITE® 2000 Valproic Acid.

Edward M. Levine 12/28/99

Edward M. Levine, Ph.D.
Director of Clinical Affairs

Date

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

MAR - 3 2000

Edward M. Levine, Ph.D.
Director of Clinical Affairs
Diagnostic Products Corporation
5700 West 96th Street
Los Angeles, California 90045-5597

Re: K000005
Trade Name: IMMULITE® Valproic Acid and IMMULITE® 2000 Valproic Acid
Regulatory Class: II
Product Code: LEG
Regulatory Class: I
Product Code: DIF
Dated: December 27, 1999
Received: January 3, 2000

Dear Dr. Levine:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known):_____

Device Name: **IMMULITE® Valproic Acid and IMMULITE® 2000 Valproic Acid**

Indications For Use:

IMMULITE Valproic Acid and IMMULITE 2000 Valproic Acid are for *in vitro* diagnostic use with their respective IMMULITE and IMMULITE 2000 Analyzers - for the quantitative measurement of valproic acid in serum or heparinized plasma, as an aid in monitoring drug therapy.

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory
510(k) Number K000015

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

✓

Prescription Use
(Per 21 CFR 801.109)

OR

Over-The-Counter Use

(Optional Format 1-2-96)